BOX PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

BECKER et al.

Serial No.: 09/718,425 Art Unit: 1634

Filed: November 24, 2000 Examiner: TAYLOR, JANELL E.

For: **METHOD AND SYSTEM FOR PREDICTING AMINO ACID SEQUENCES COMPATIBLE WITH A SPECIFIED THREE DIMENSIONAL STRUCTURE**

Appendix B

Please amend claim 1 and add new claim 23 as outlined in the following "clean" copy of the claims.

1. A computer-implemented method for predicting at least one amino acid sequence compatible with a specified three-dimensional (3D) structure of a protein or peptide; which method comprises the steps of:
   a. providing a coordinate set representing the backbone of said 3D structure;
   b. constructing a reduced virtual representation for the 3D structure provide in step (a);
   c. determining for each position along the virtual structure representation provided in step (b) its solvent accessibility;
   d. constructing an initial amino acid sequence by randomly assigning for each position along the structure an amino acid residue selected randomly from a predefined group

of amino acids having a solvent accessibility compatible with the solvent accessibility of said position;

e. randomly selecting one or more positions along the sequence provided in step (d) and applying on each position a Monte-Carlo simulation in sequence space and rotamer space, said simulation comprising one or more scoring function calculating steps which include:

i. randomly selecting one or more amino acid residues of the same solvent accessibility as that defined for said position to obtain a mutation;

ii. calculating an energy scoring function for each possible rotamer of each amino acid residue provided in step (i) based on their said reduced virtual representation;

iii. selecting the lowest scoring rotamer or when more than one amino acid is manipulated simultaneously, selecting the lowest scoring rotamer combination;

iv. determining whether to accept or reject the mutation with the rotamer or rotamer combination selected in step (iii); and

v. assigning the amino acid residue or residues and their respective selected rotamer or rotamer combinations selected in step (iii) to said position/s and moving to another position along the

sequence;

said simulation steps are repeated until for each position along said sequence, the residue and residue's rotamer with the lowest energy score is selected, to obtain a virtually represented amino acid sequence with the lowest total energy score;

f. expanding the reduced representation of the virtually represented amino acid sequence obtained in step (e) to its corresponding all-atom sequence representation thereby obtaining an amino acid sequence compatible with the predefined 3D structure;

g. optionally, creating a computer output of the expanded all-atom representation of the primary structure/s obtained in step (f).

32. A means for practicing the method of claim 1, comprising: a computer based system for predicting at least one amino acid sequence compatible with a specified three-dimensional (3D) structure of a protein or peptide, said system comprising:

a. input apparatus for specifying said 3D structure;

b. a first memory for storing the specified 3D structure;

c. a second memory having stored thereon an application program which when running, provides at least one amino acid sequence compatible with the specified 3D structure;

d. a third memory for storing the at least one amino acid sequence obtained;

e. a processor coupled to said input means, and to said first, second and third memories for representation of said amino acid sequence; and

f. optionally, a display unit coupled to said processing means for displaying the amino acid sequence.